Amendments to the Claims

Please cancel Claims 4, 5, 8, 30, 31, 34 and 55.

1. (Currently amended) A method comprising:
contacting a preparation of a recombinant ~~protein~~ soluble form of a TNF-receptor that has been produced by mammalian cells with a reduction/oxidation coupling reagent, at a pH of about 7 to about 11, and isolating a fraction of the preparation of the recombinant ~~protein~~ soluble form of the TNF-receptor with a desired conformation.

2. (Original) The method of claim 1 wherein the recombinant protein contains at least two domains.

3. (Original) The method of claim 2 wherein at least one domain of the protein has a stable conformation, and at least one domain of the protein has an unstable conformation.

Claims 4 and 5 are cancelled.

6. (Currently amended) The method of claim 1 wherein the recombinant soluble form of the TNF-receptor~~protein~~ is a Fc fusion protein.

7. (Currently amended) The method of claim 6 wherein the preparation of the recombinant soluble form of the TNF-receptor~~protein~~ has been purified from a Protein A or Protein G column.

Claim 8 is cancelled

9. (Original) The method of claim 1 wherein the pH is from about 7 to about 10.

10. (Original) The method of claim 9 wherein the pH is about 7.6 to about 9.6.

11. (Original) The method of claim 10, wherein the pH is about 8.6.

12. (Original) The method of claim 1 wherein the reduction/oxidation coupling reagent comprises glutathione.

13. (Original) The method of claim 12 wherein the ratio of reduced glutathione to oxidized glutathione is about 1:1 to about 100:1.

14. (Original) The method of claim 1 wherein the reduction/oxidation coupling reagent comprises cysteine.

15. (Original) The method of claim 1 wherein the contacting step is performed for about 4 to about 16 hours.

16. (Original) The method of claim 1 wherein the contacting step is performed at about 25°C.

17. (Original) The method of claim 1 wherein the contacting step is performed at about 4°C.

18. (Original) The method of claim 1 wherein the contacting step is quenched by acidification.

19. (Original) The method of claim 1 wherein the isolating step comprises one or more chromatography steps.

20. (Currently amended) The method of claim 1 wherein the protein concentration of the recombinant soluble form of the TNF-receptor is from about 0.5 to about 10 mg/ml.

21. (Original) The method of claim 1 wherein the ratio of reducing thiols in the reduction/oxidation coupling reagent to disulfide bonds in the protein is about 320:1 to about 64,000:1 (reducing thiols: disulfide bond).

22. (Currently amended) The method of claim 1 further comprising formulating the fraction of the preparation of the recombinant soluble form of the TNF-receptor~~protein~~ with the desired conformation in a sterile bulk form.

23. (Currently amended) The method of claim 1 further comprising formulating the fraction of the preparation of the recombinant soluble form of the TNF-receptor~~protein~~ with the desired conformation in a sterile unit dose form.

24. (Currently amended) The method of claim ~~4~~ 1 wherein the desired conformation has a higher binding affinity for a cognate ligand of the TNF-receptor.

25. (Currently amended) The method of claim ~~5~~ 24 wherein the desired conformation has a higher binding affinity for TNF.

26. (Original) The method of claim 25 wherein the TNF is TNF-alpha.

27. (Currently amended) A method of promoting a desired conformation of a glycosylated recombinant soluble form of the TNF-receptor~~protein~~, the method comprising

contacting a preparation of the glycosylated recombinant soluble form of the TNF-receptor~~protein~~ that contains a mixture of at least two configurational isomers of the glycosylated recombinant soluble form of the TNF-receptor~~protein~~ with a reduction/oxidation coupling reagent for a time sufficient to increase the relative proportion of the desired configurational isomer and

determining the relative proportion of the desired configurational isomer in the mixture.

28. (Currently amended) The method of claim 27 wherein the glycosylated recombinant soluble form of the TNF-receptor~~protein~~ contains at least two domains.

29. (Currently amended) The method of claim 28 wherein at least one domain of the glycosylated recombinant soluble form of the TNF-receptor ~~protein~~ has a stable conformation, and at least one domain of the glycosylated recombinant soluble form of the TNF-receptor ~~protein~~ has an unstable conformation.

Claims 30 and 31 are cancelled.

32. (Currently amended) The method of claim 27 wherein the glycosylated recombinant soluble form of the TNF-receptor~~protein~~ is a Fc fusion protein.

33. (Currently amended) The method of claim 32 wherein the preparation of the glycosylated recombinant soluble form of the TNF-receptor ~~protein~~ has been purified from a Protein A or Protein G column.

Claim 34 is cancelled.

35. (Original) The method of claim 27 wherein the pH is from about 7 to about 10.

36. (Original) The method of claim 35 wherein the pH is about 8.6.

37. (Original) The method of claim 27 wherein the reduction/oxidation coupling reagent is selected from the group consisting of glutathione, cysteine, DTT (dithiothreitol), 2-mercaptoethanol and dithionitrobenzoate.

38. (Original) The method of claim 37 wherein the reduction/oxidation coupling reagent comprises reduced glutathione.

39. (Original) The method of claim 38 wherein the reduced glutathione is at a concentration of about 1 mM to about 10 mM.

40. (Original) The method of claim 37 wherein the reduction/oxidation coupling reagent comprises reduced cysteine.

41. (Original) The method of claim 37 wherein the ratio of reducing thiols in the reduction/oxidation coupling reagent to disulfide bonds in the protein is about 320:1 to about 64,000:1 (reducing thiols: disulfide bond).

42. (Original) The method of claim 27 wherein the protein concentration is from about 0.5 to about 10 mg/ml.

43. (Original) The method of claim 27 wherein the contacting step is performed for about 4 to about 16 hours.

44. (Original) The method of claim 27 wherein the contacting step is performed at about 25°C.

45. (Original) The method of claim 27 wherein the contacting step is performed at about 4°C.

46. (Original) The method of claim 27 wherein the contacting step is quenched by acidification.

47. (Original) The method of claim 27 wherein the determining step comprises one or more chromatography steps.

48. (Original) The method of claim 27 wherein the determining step comprises a binding reaction.

49. (Currently amended) The method of claim 27 comprising isolating a fraction of the preparation of the glycosylated recombinant soluble form of the TNF-receptor ~~protein~~ with the desired configurational isomer.

50. (Original) The method of claim 49 comprising formulating the desired configurational isomer in a sterile unit dose form.

51. (Currently amended) The method of claim ~~30~~ 27 wherein the desired configurational isomer has a higher binding affinity for a cognate ligand of the receptor.

52. (Currently amended) The method of claim ~~31~~ 51 wherein the desired configurational isomer has a higher binding affinity for TNF.

53. (Original) The method of claim 52 wherein the TNF is TNF-alpha.

54. (Currently amended) A method comprising formulating into sterile unit dose form a recombinant soluble form of the TNF-receptor ~~protein~~ that has been produced by mammalian cells, contacted with a reduction/oxidation coupling reagent, and isolated from the fraction of the protein with an undesired conformation.

Claim 55 is cancelled.

56. (New) The method of claim 1 wherein the contacting step is performed in a solution essentially free of chaotrope.

57. (New) The method of claim 27 wherein the contacting step is performed in a solution essentially free of chaotrope.

58. (New) The method of claim 54 wherein the contacting step has been performed in a solution essentially free of chaotrope.

59. (New) The method of claim 6 wherein the recombinant soluble form of the TNF-receptor is the p75 TNFR.

60. (New) The method of claim 32 wherein the recombinant soluble form of the TNF-receptor is the p75 TNFR.

61. (New) The method of claim 54 wherein the recombinant soluble form of the TNF-receptor is the p75 TNFR.